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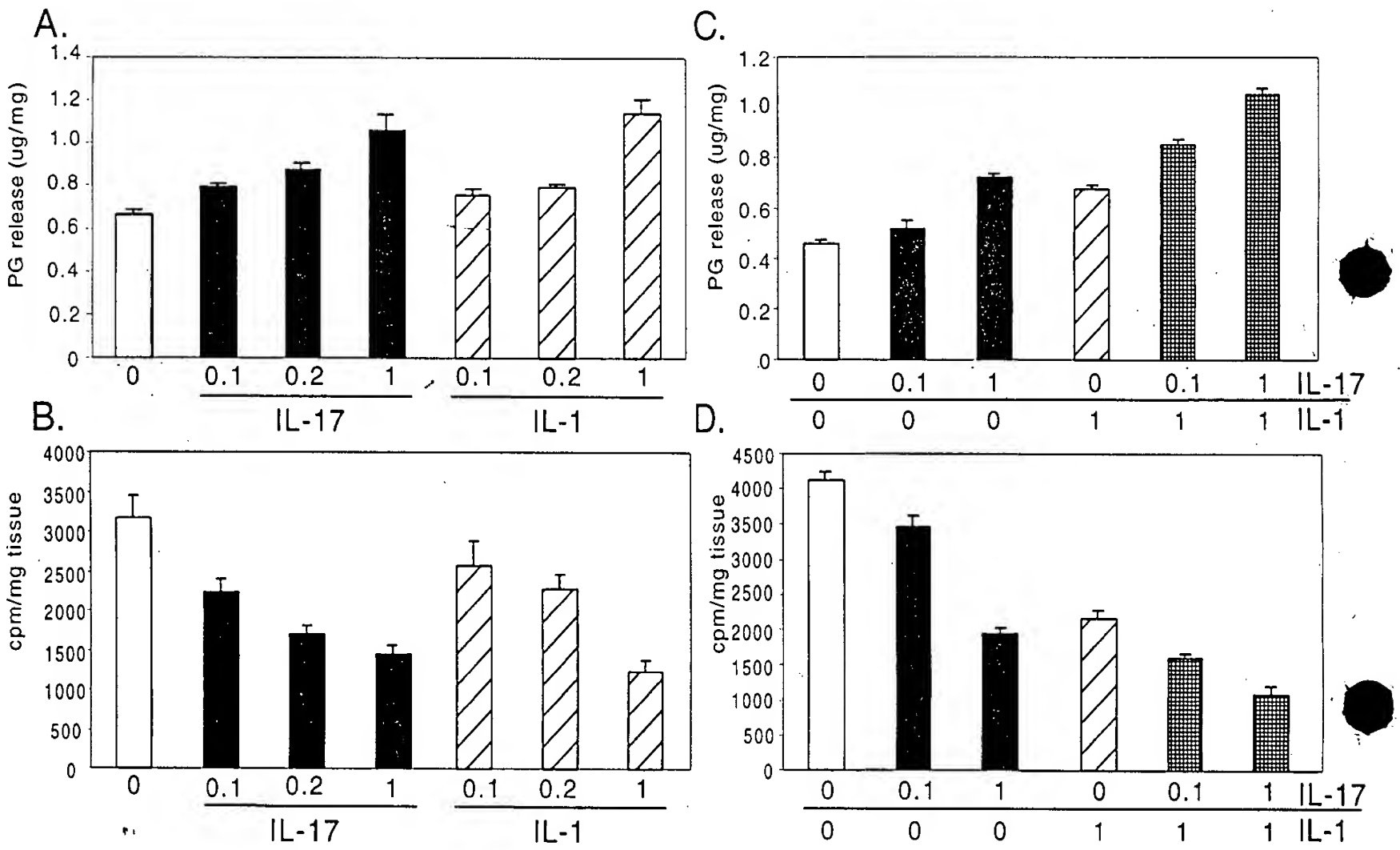

A.
PG release (ug/mg)
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0
0
0.1
0.2
1
0.1
0.2
1
IL-17
IL-1
C.
PG release (ug/mg)
1.2
1.0
0.8
0.6
0.4
0.2
0
0
0.1
1
0
0.1
1
IL-17
0
0
0
1
1
1
IL-1
B.
cpm/mg tissue
4000
3500
3000
2500
2000
1500
1000
500
0
0
0.1
0.2
1
0.1
0.2
1
IL-17
IL-1
D.
cpm/mg tissue
4500
4000
3500
3000
2500
2000
1500
1000
500
0
0
0.1
1
0
0.1
1
IL-17
0
0
0
1
1
1
IL-1

Figure 1

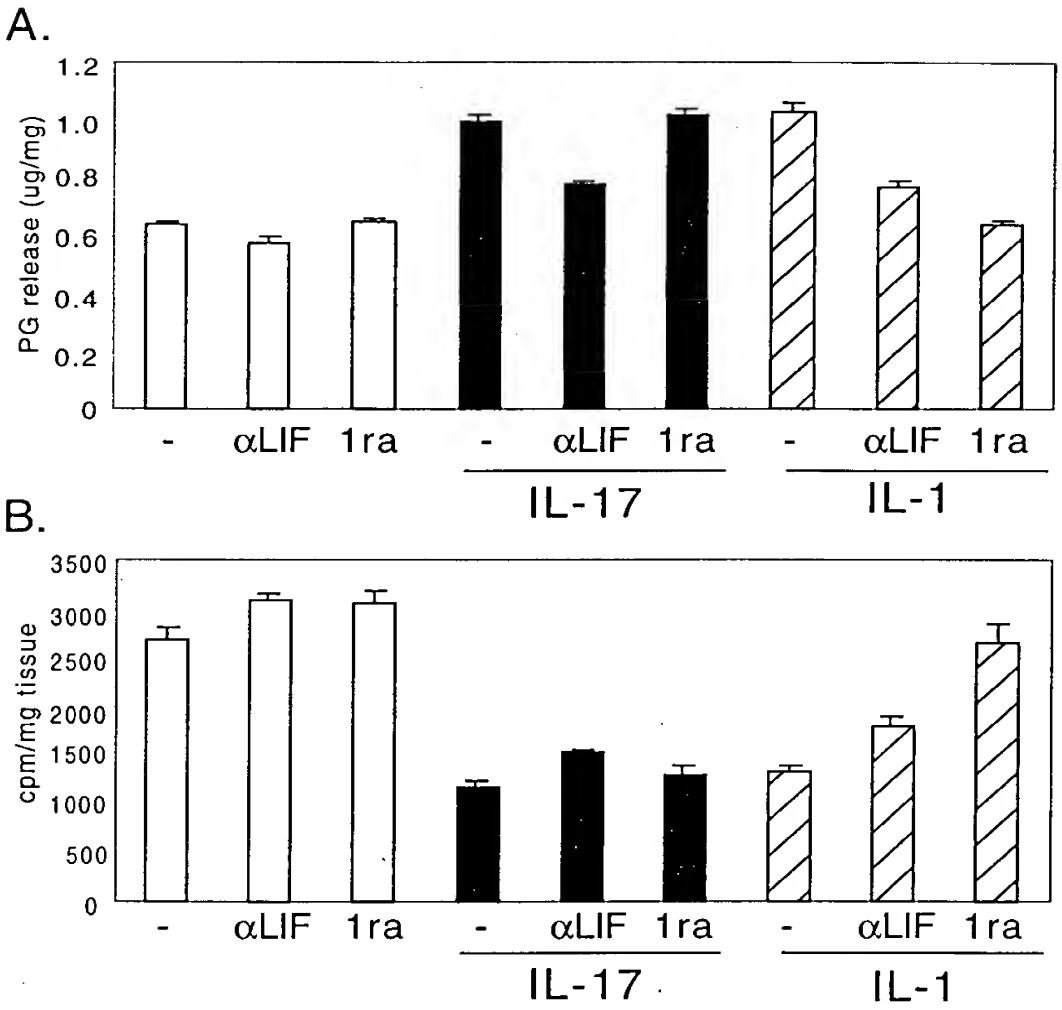

A.
PG release (ug/mg)
1.2
1.0
0.8
0.6
0.4
0.2
0
-
αLIF
1ra
-
αLIF
1ra
-
αLIF
1ra
IL-17
IL-1
B.
cpm/mg tissue
3500
3000
2500
2000
1500
1000
500
0
-
αLIF
1ra
-
αLIF
1ra
-
αLIF
1ra
IL-17
IL-1

Figure 2

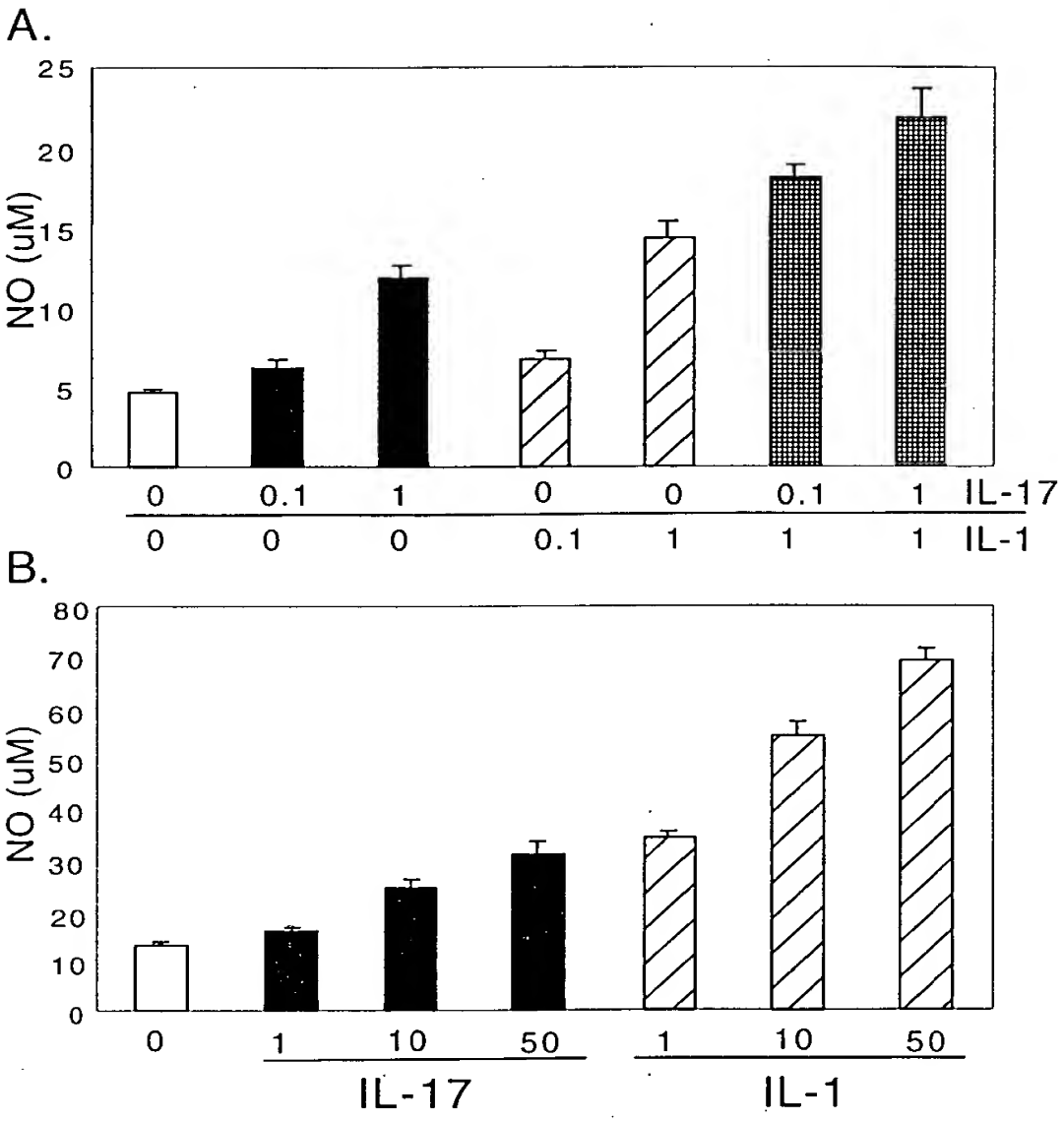

A.
NO (uM)
25
20
15
10
5
0
0 0.1 1 0 0 0.1 1 IL-17
0 0 0 0.1 1 1 1 IL-1
B.
NO (uM)
80
70
60
50
40
30
20
10
0
0 1 10 50 1 10 50
IL-17
IL-1

Figure 3

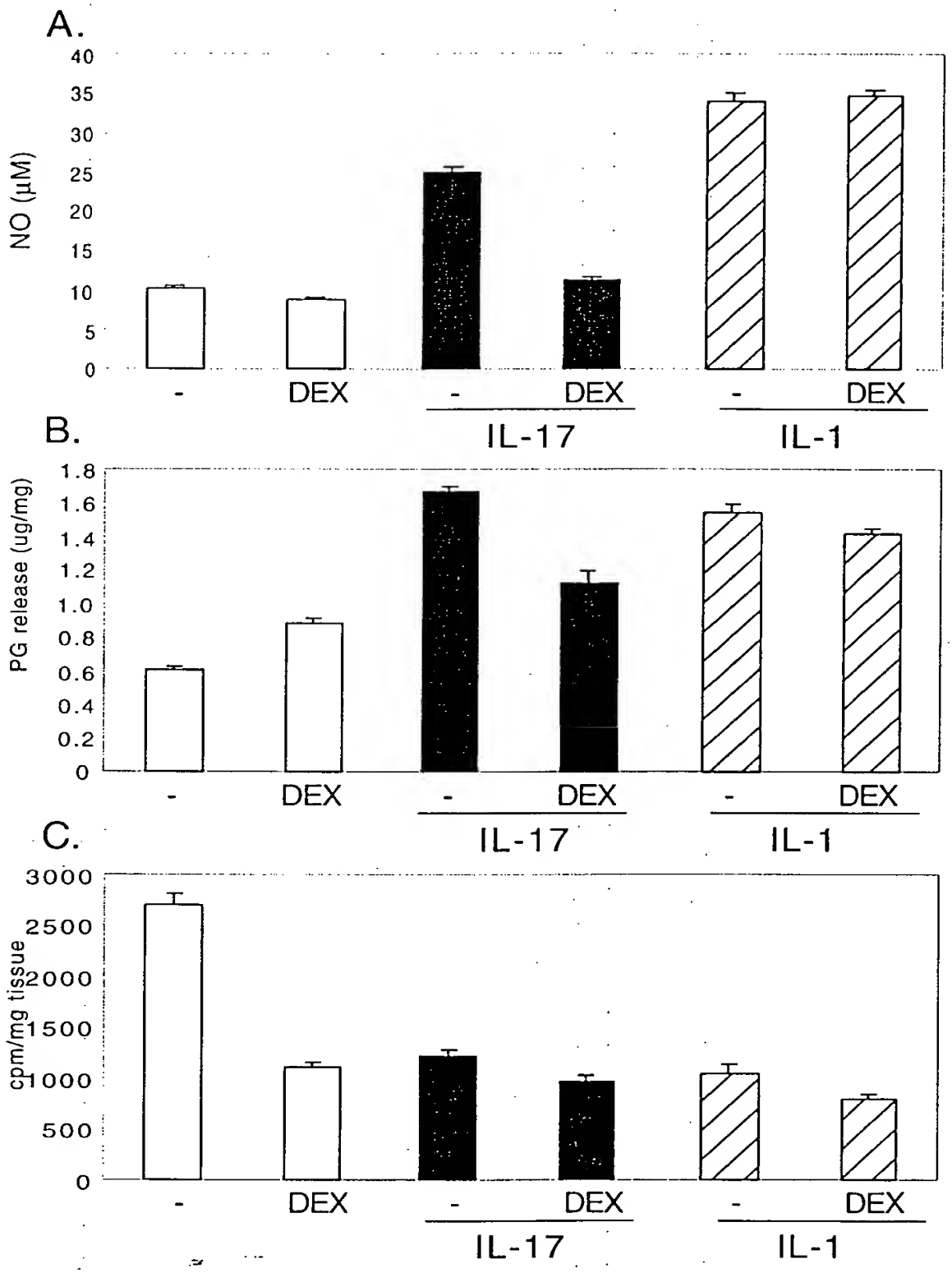

A.
NO (μM)
40
35
30
25
20
15
10
5
0
-
DEX
-
DEX
-
DEX
IL-17
IL-1
B.
PG release (ug/mg)
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0
-
DEX
-
DEX
-
DEX
IL-17
IL-1
C.
cpm/mg tissue
3000
2500
2000
1500
1000
500
0
-
DEX
-
DEX
-
DEX
IL-17
IL-1

Figure 4

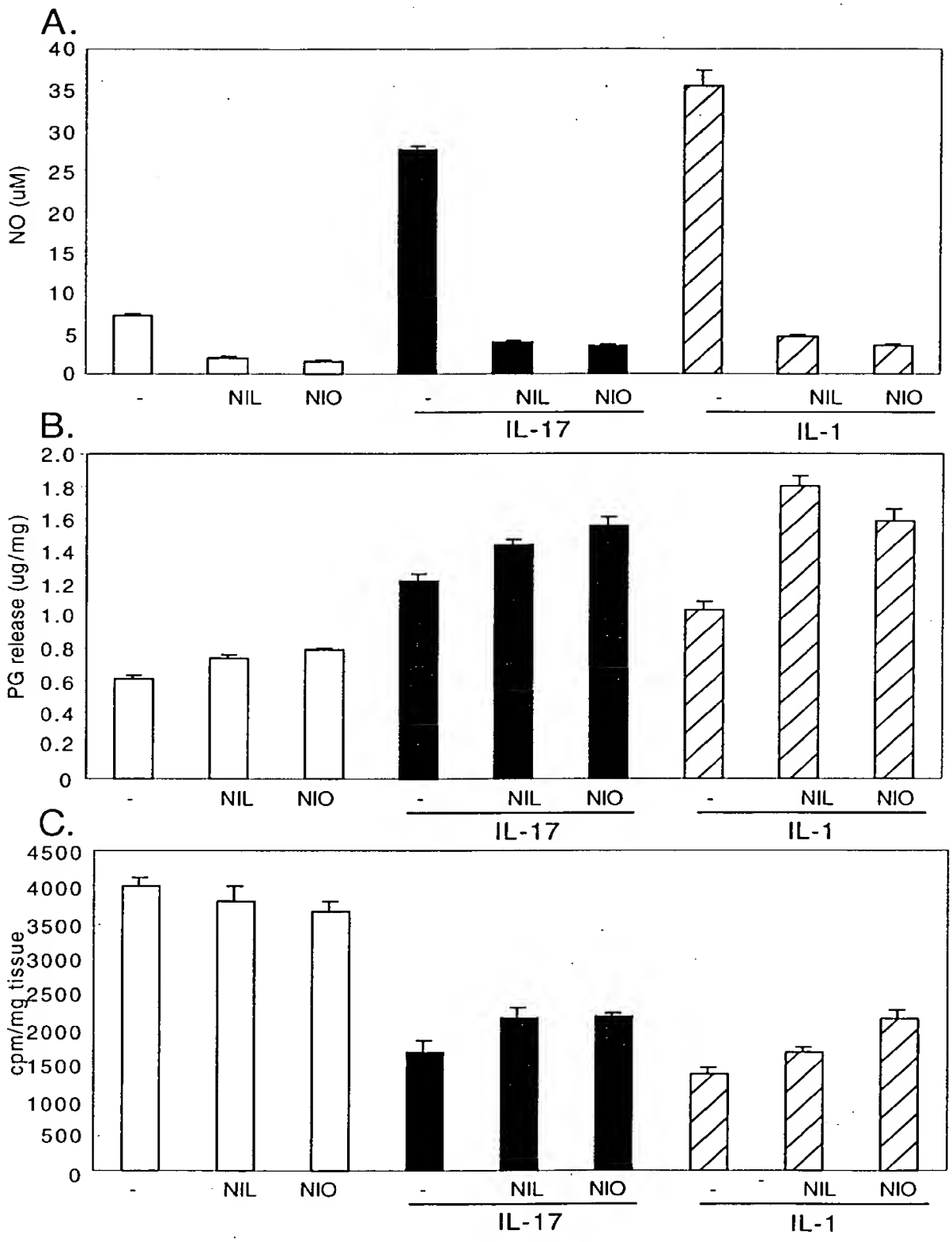

A.
NO (uM)
40
35
30
25
20
15
10
5
0
-
NIL
NIO
-
NIL
NIO
-
NIL
NIO
IL-17
IL-1
B.
PG release (ug/mg)
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0
-
NIL
NIO
-
NIL
NIO
-
NIL
NIO
IL-17
IL-1
C.
cpm/mg tissue
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-
NIL
NIO
-
NIL
NIO
-
NIL
NIO
IL-17
IL-1

Figure 5

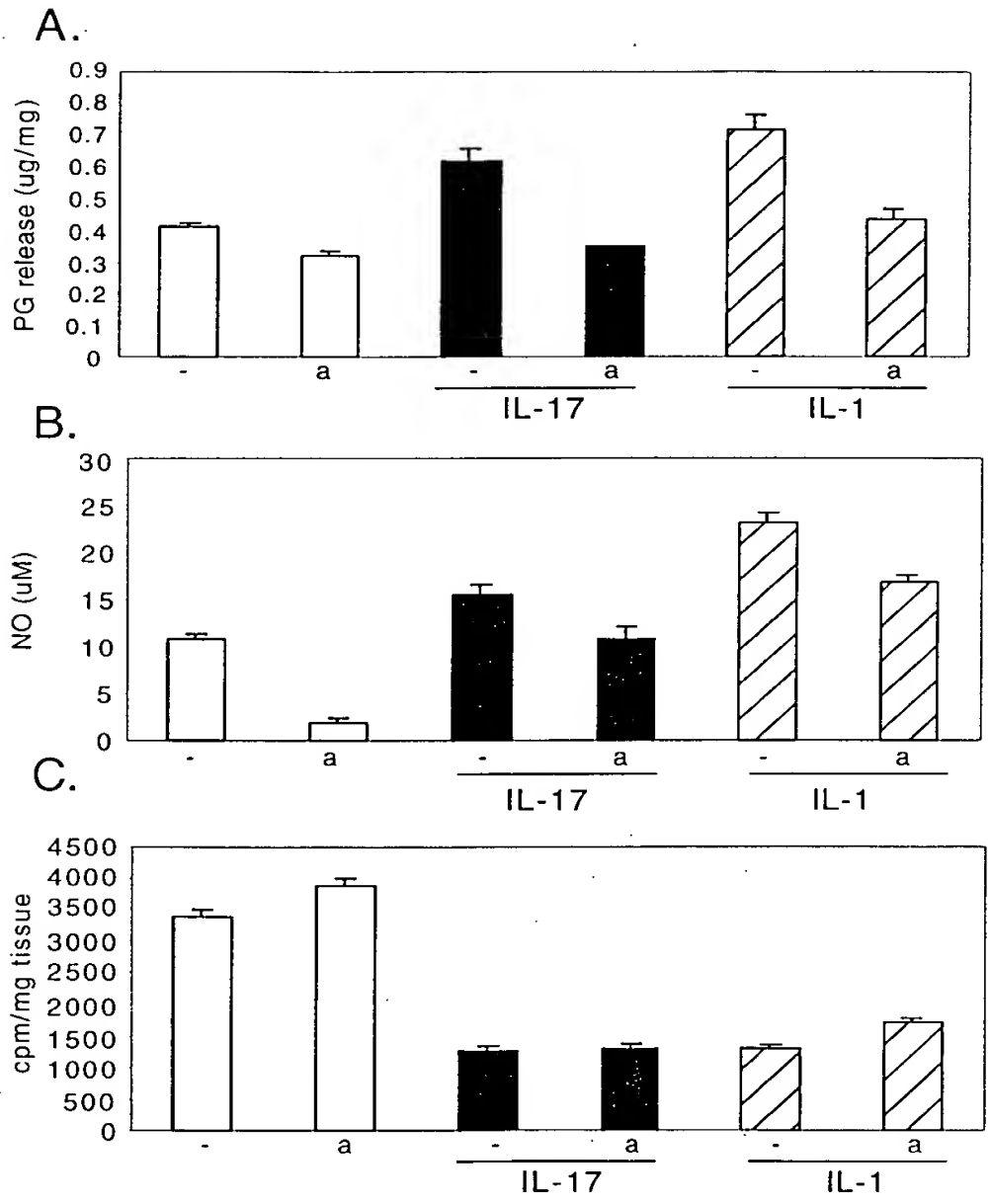

A.
PG release (ug/mg)
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
-
a
-
a
-
a
IL-17
IL-1
B.
NO (uM)
30
25
20
15
10
5
0
-
a
-
a
-
a
IL-17
IL-1
C.
cpm/mg tissue
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-
a
-
a
-
a
IL-17
IL-1

Figure 6

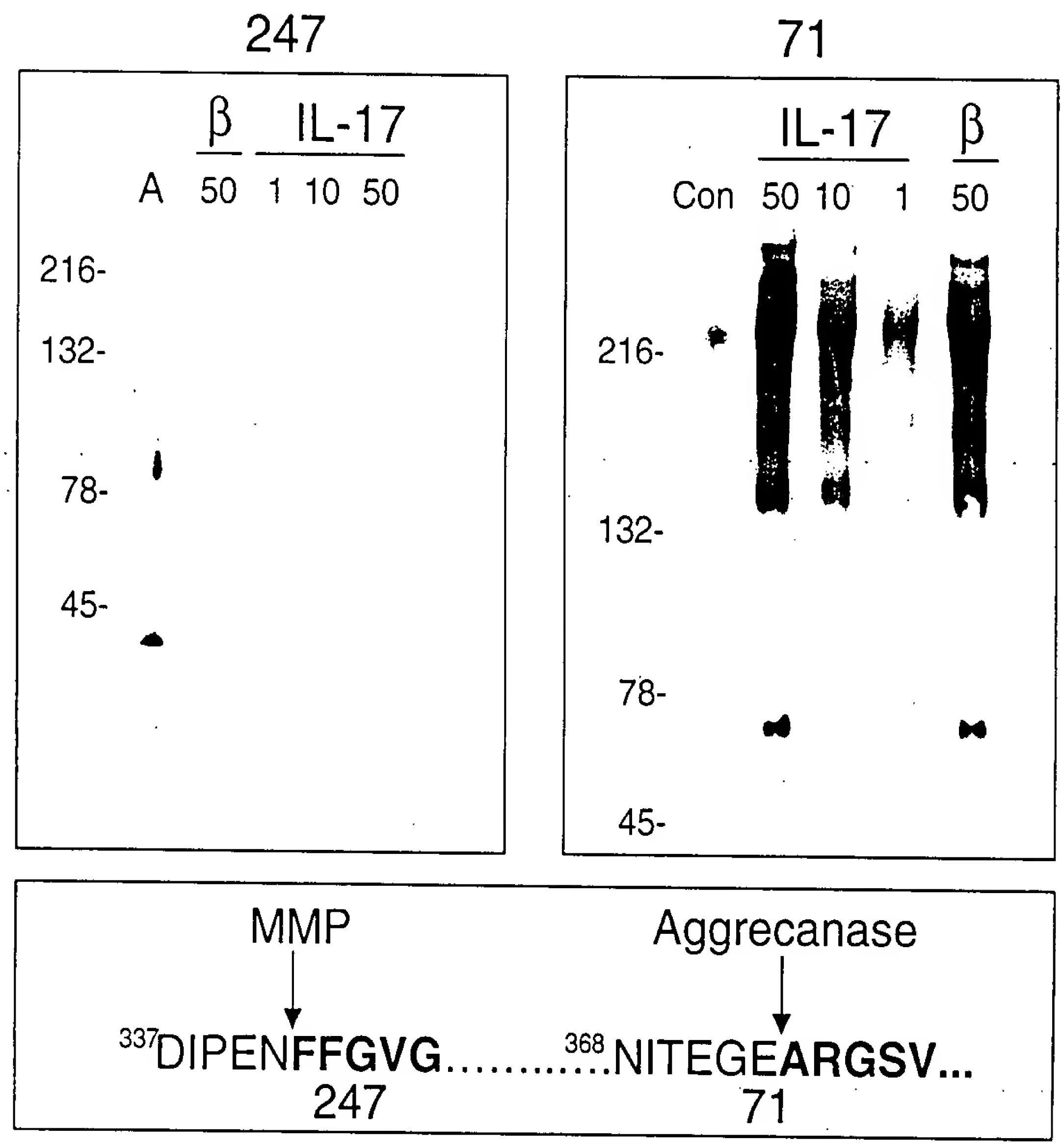

247
β
IL-17
A
50
1
10
50
216-
132-
78-
45-
71
IL-17
β
Con
50
10
1
50
216-
132-
78-
45-
MMP
Aggrecanase
337DIPENFFGVG............368NITEGEARGSV...
247
71

Figure 7

Effect of interleukins on MMPs

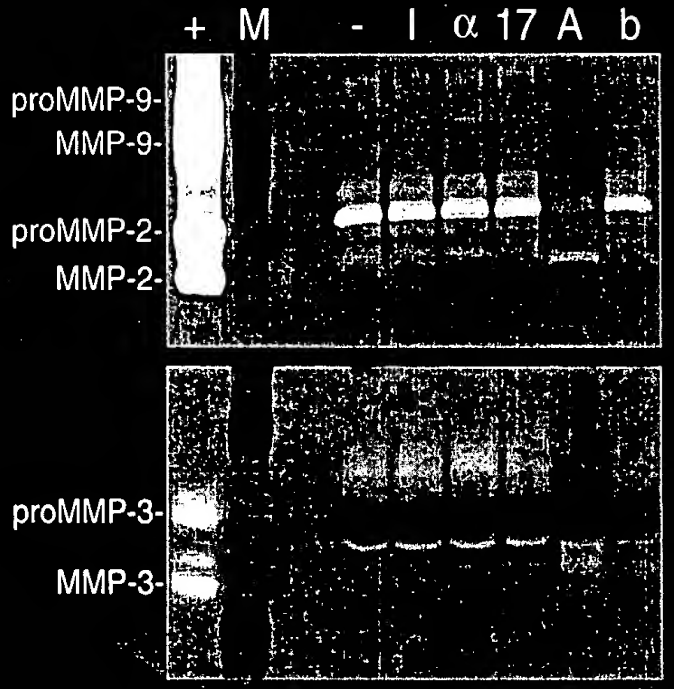


FIG. 8

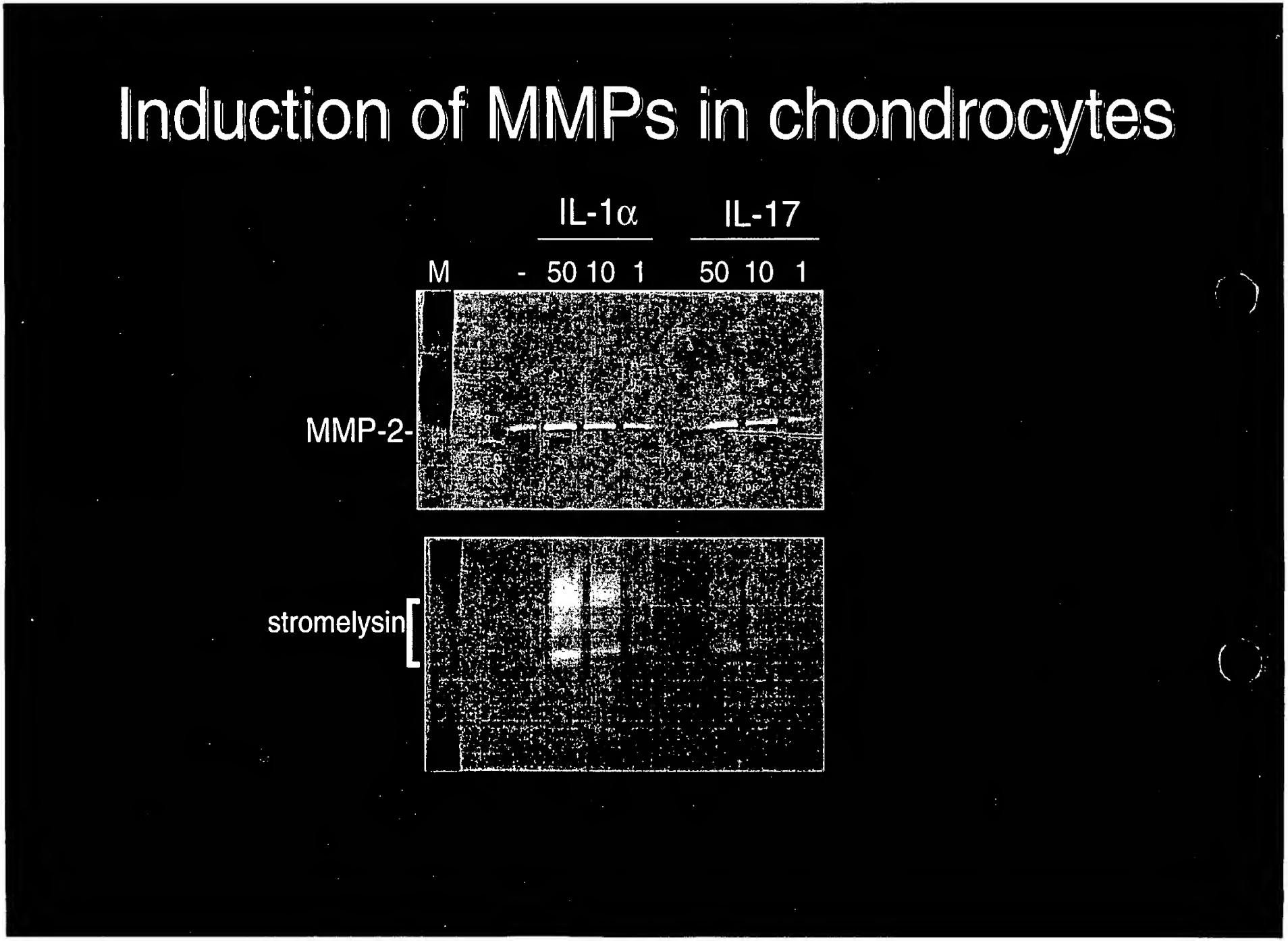
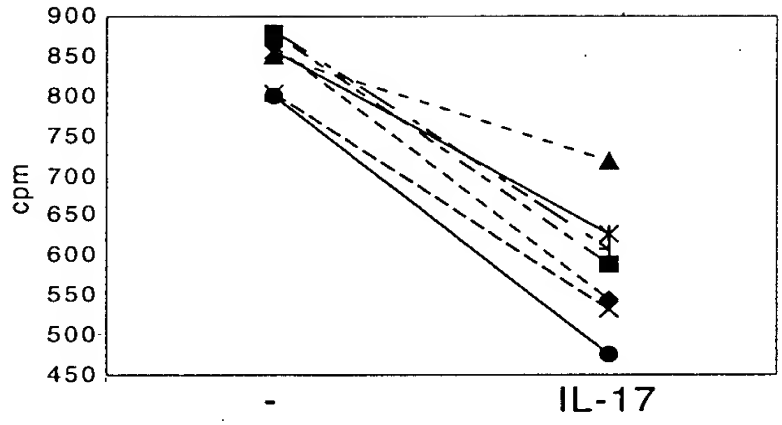

Induction of MMPs in chondrocytes
IL-1α
IL-17
M
-
50
10
1
50
10
1
MMP-2-
stromelysin

FIG. 9

A.


900
850
800
750
700
650
600
550
500
450
cpm
-
IL-17

B.

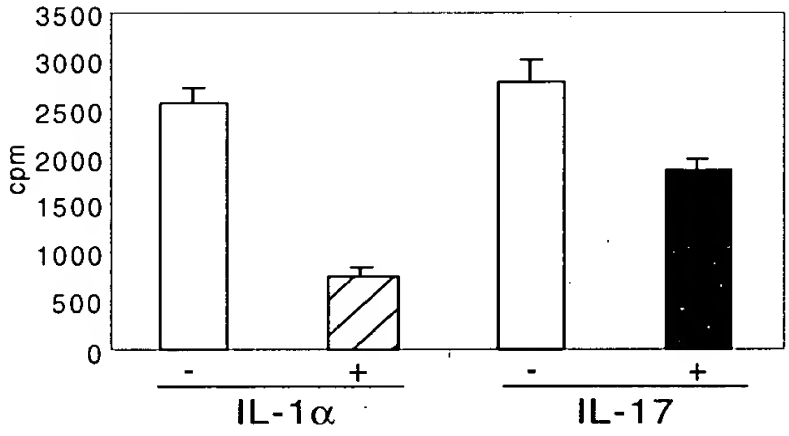

3500
3000
2500
2000
1500
1000
500
0
cpm
-
+
-
+
IL-1α
IL-17

Figure 10

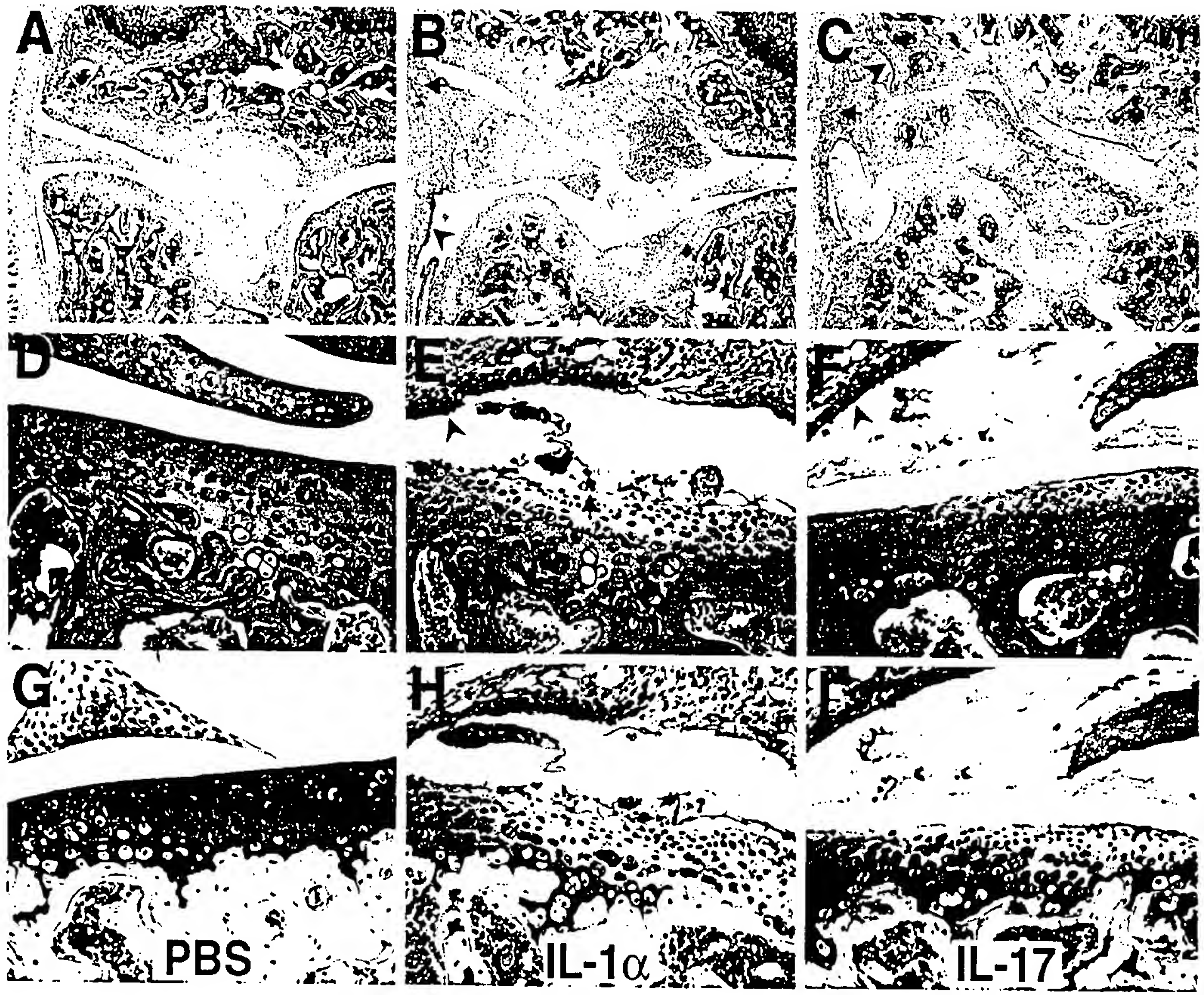


FIG. 11

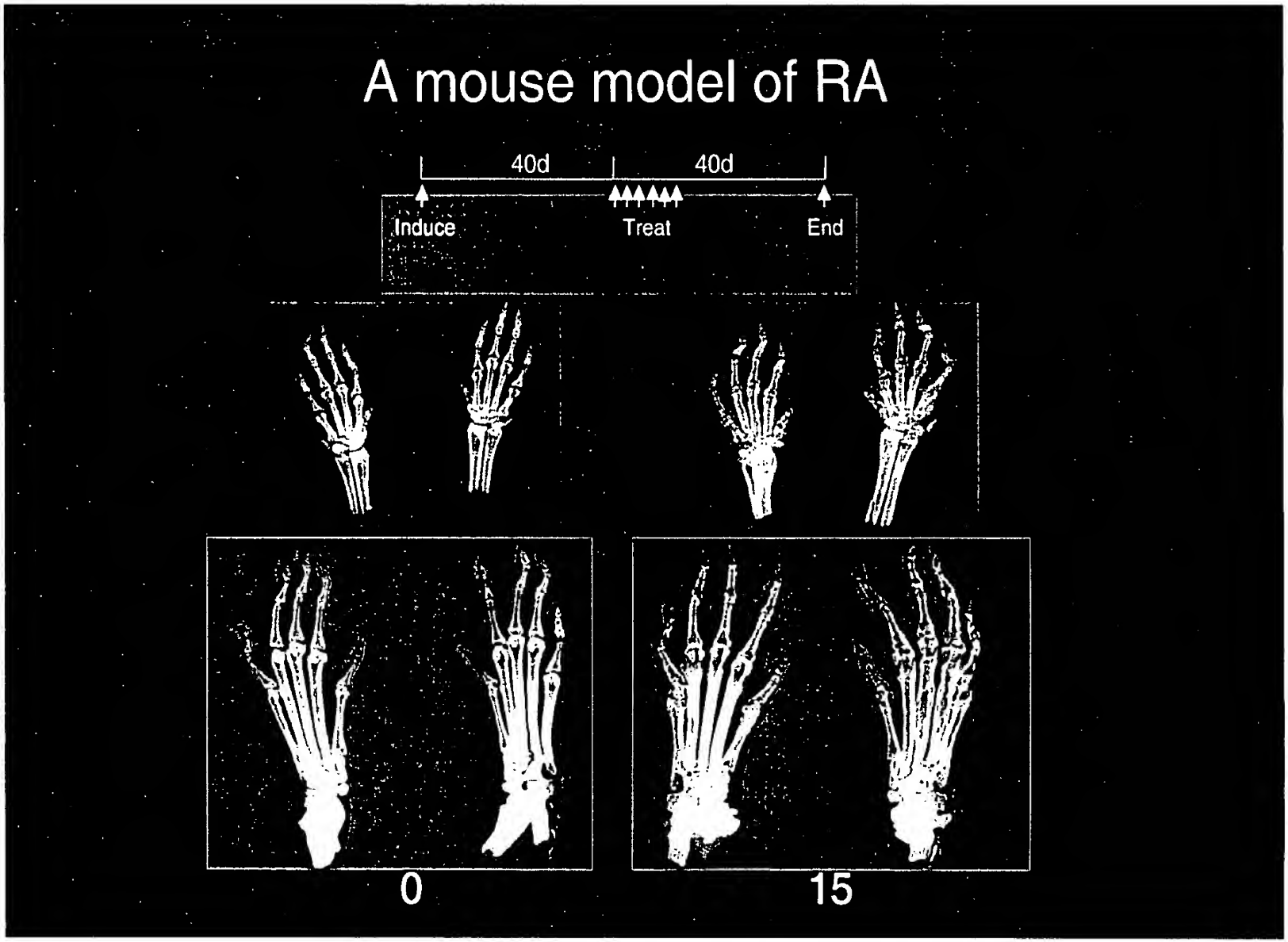


FIG. 12

Effect of anti-IL-17 in an RA model

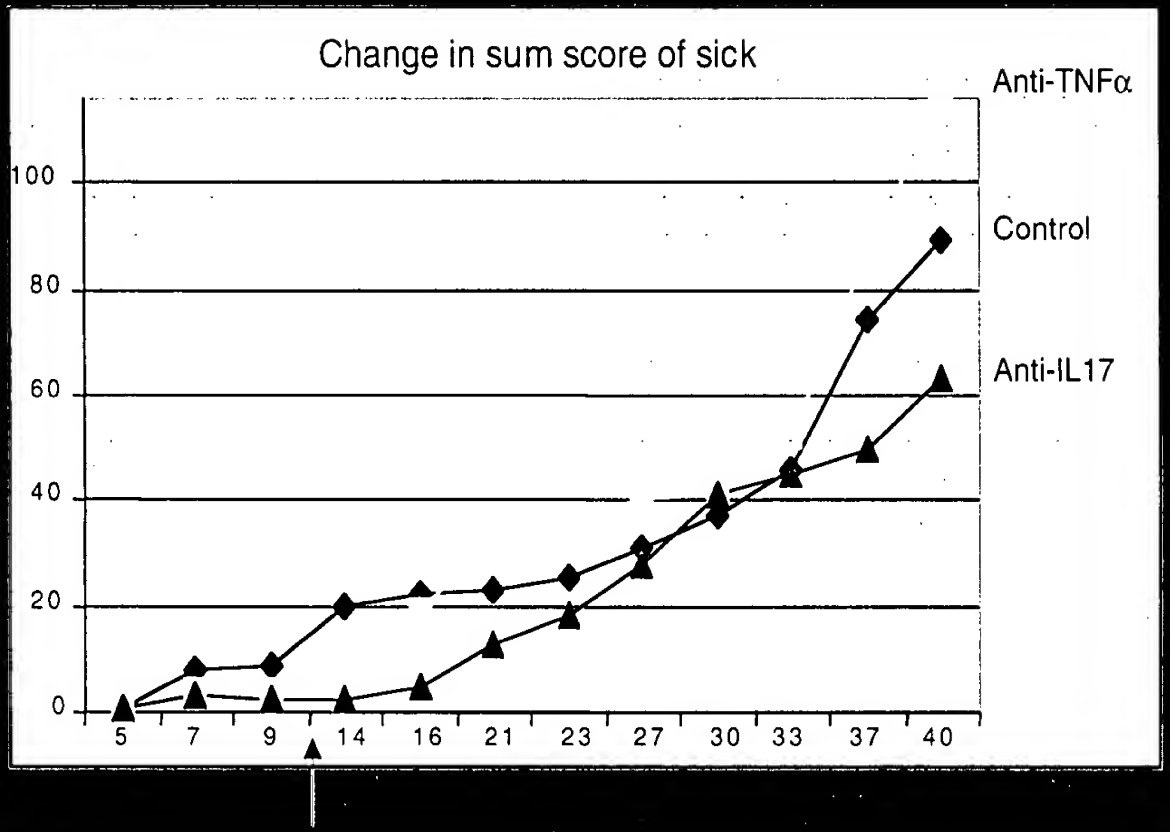


FIG. 13

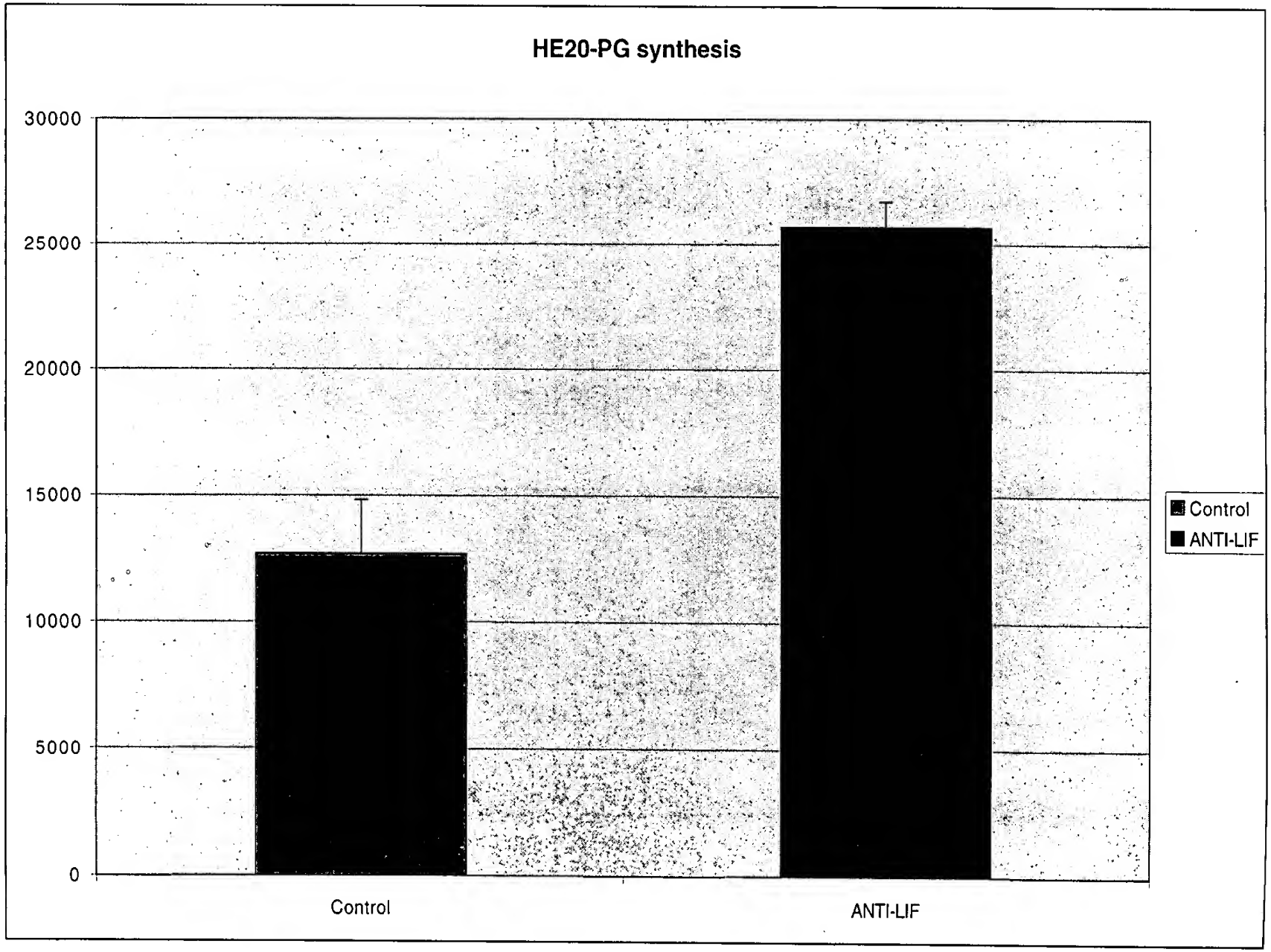

HE20-PG synthesis
30000
25000
20000
15000
10000
5000
0
Control
ANTI-LIF
Control
ANTI-LIF

FIG. 14

IL-17 induces breakdown and inhibits synthesis of cartilage matrix

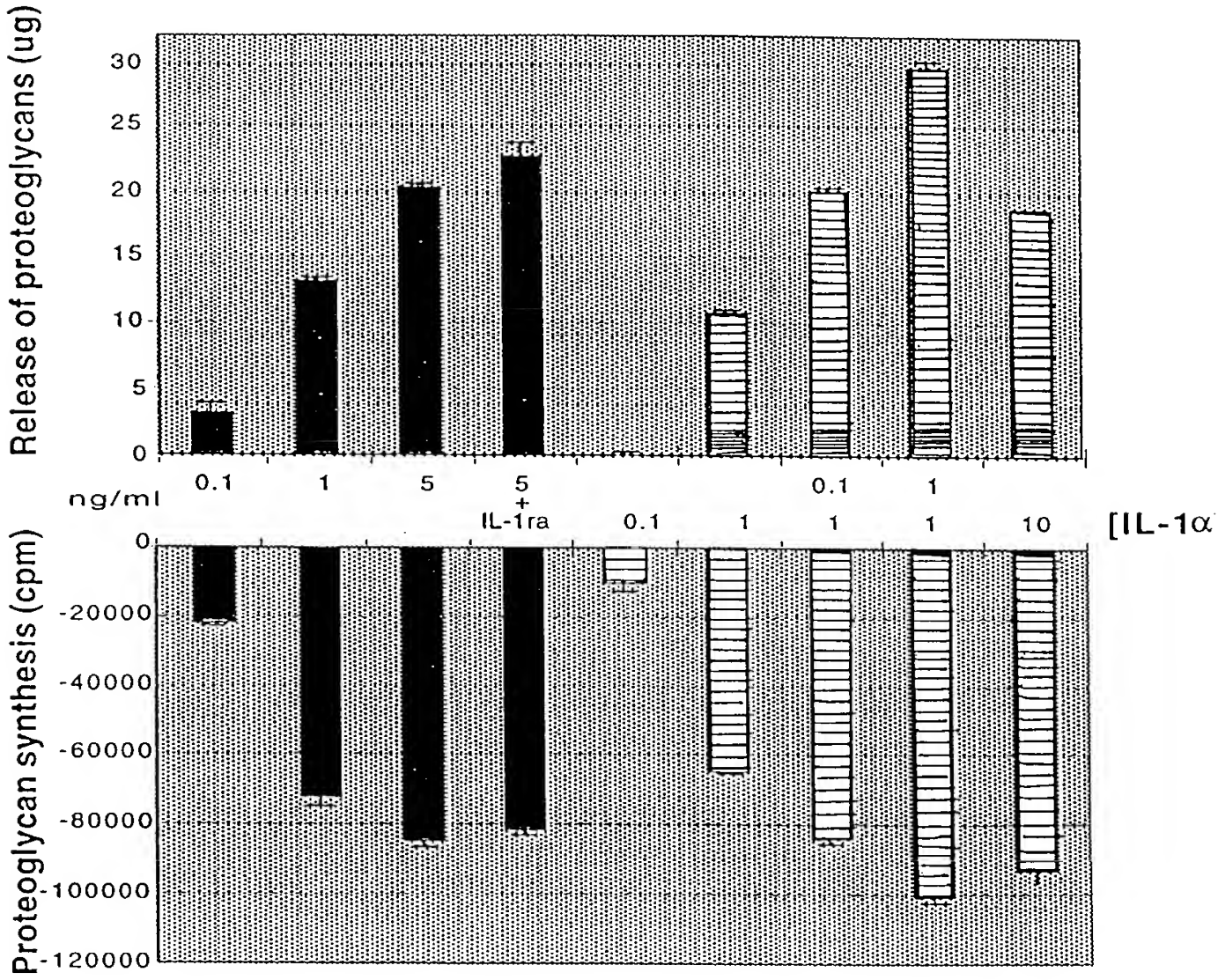


FIG. 15

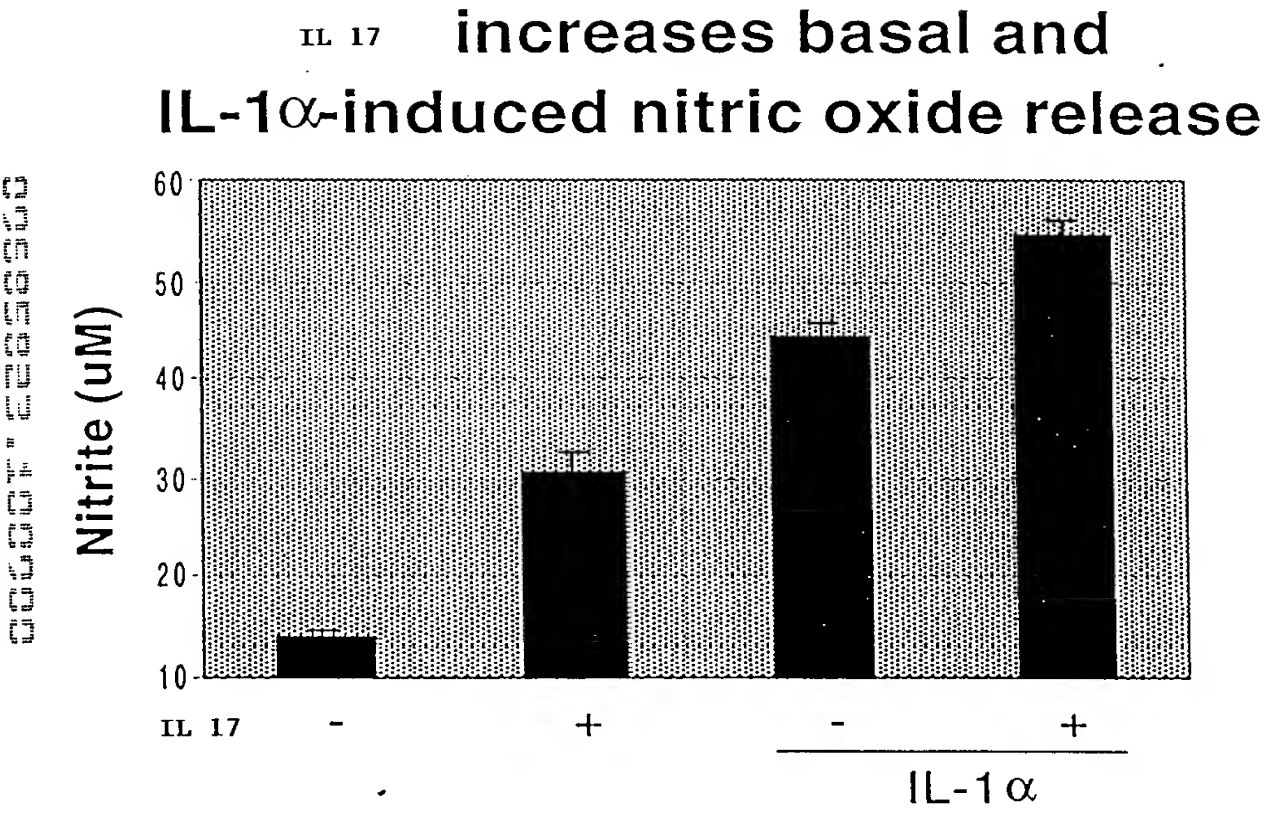

IL 17 increases basal and
IL-1α-induced nitric oxide release
Nitrite (uM)
60
50
40
30
20
10
IL 17
-
+
-
+
IL-1α

FIG. 16

Inhibition of nitric oxide release does not block the detrimental effects of IL 17 on matrix breakdown or synthesis

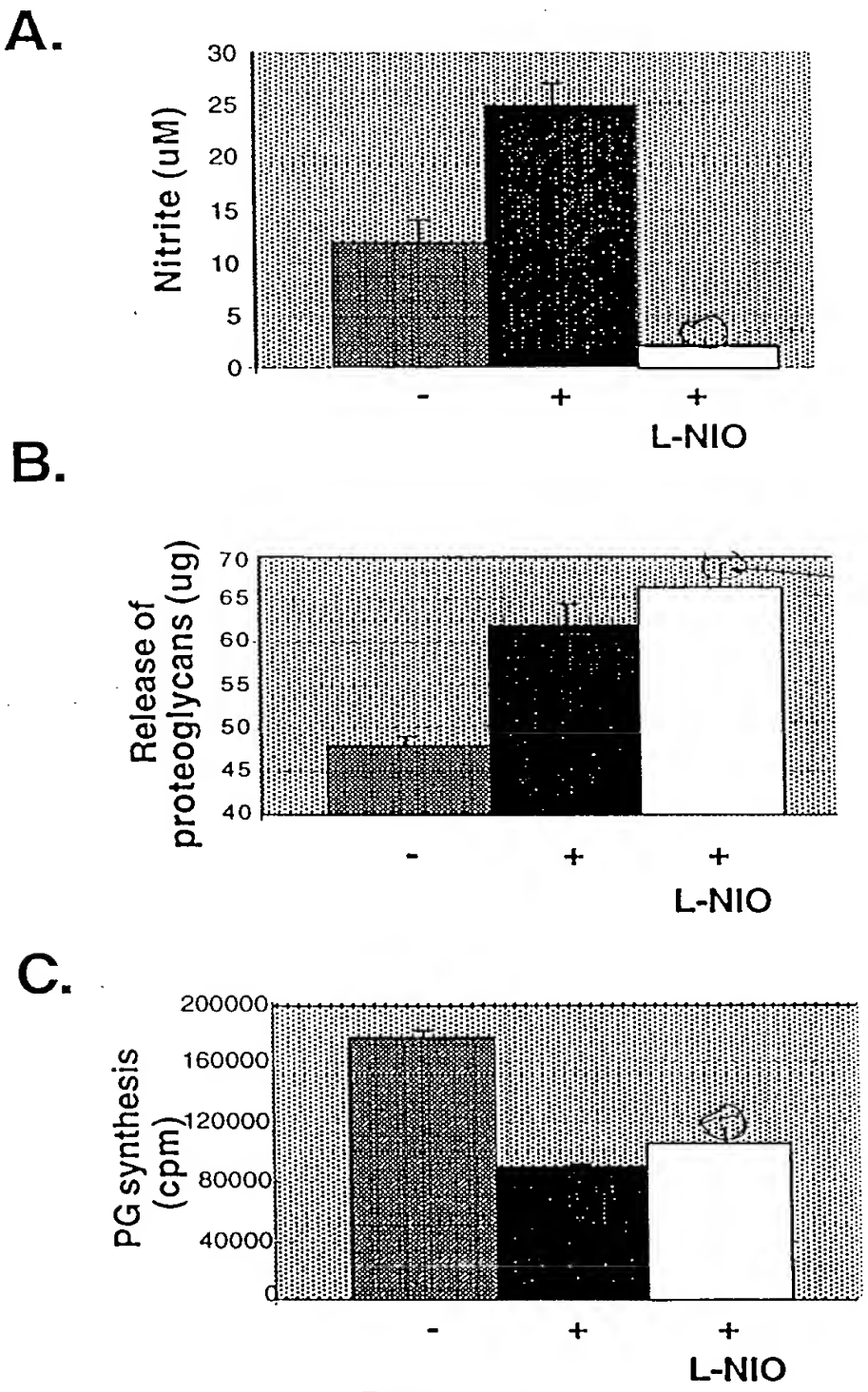


FIG. 17

INHIBITION of NO release enhances IL1-α-induced matrix breakdown but not matrix synthesis

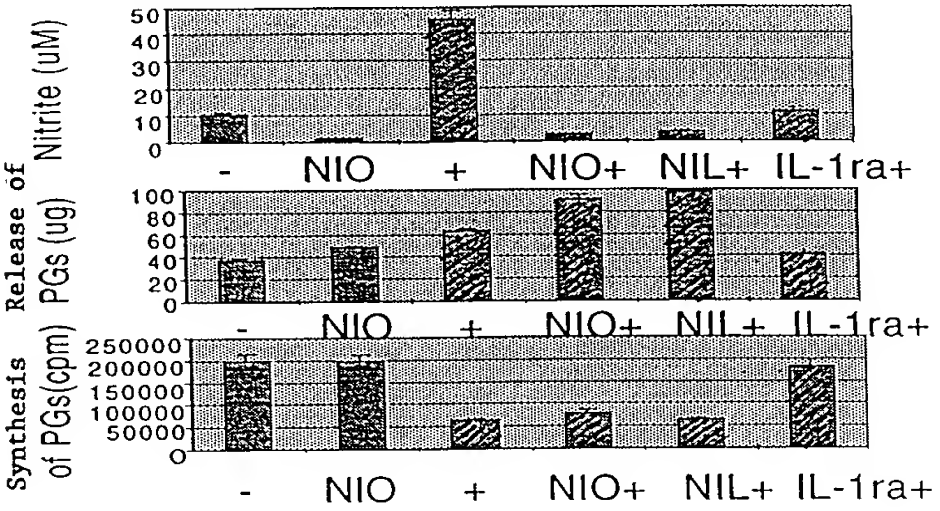


FIG. 18